DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

March 31, 2015

SIEMENS HEALTHCARE DIAGNOSTICS INC.
FATIMA PACHECO
REGULATORY CLINICAL AFFAIRS SPECIALIST
511 BENEDICT AVENUE
TARRYTOWN NY 10591-5097

Re: K142723
Trade/Device Name: ADVIA Centaur® Cortisol (COR) Assay
Regulation Number: 21 CFR 862.1205
Regulation Name: Cortisol (hydrocortisone and hydroxycorticosterone) test system
Regulatory Class: II
Product Code: JFT
Dated: February 18, 2015
Received: February 19, 2015

Dear Ms. Fatima Pacheco:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Katherine Serrano -S

For: Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k142723

Device Name
ADVIA Centaur® Cortisol (COR) Assay

Indications for Use *(Describe)*
The ADVIA Centaur® Cortisol (COR) Assay is for in vitro diagnostic use in the quantitative determination of cortisol in serum or urine using the ADVIA Centaur XP system. Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

510(k) Summary of Safety and Effectiveness

Introduction: According to the requirements of SMDA 1990 and 21 CFR 807.92, the following information provides sufficient details to understand the basis for determination of substantial equivalence.

The assigned 510(k) Number: k142723

I. SUBMITTER

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue,
Tarrytown, NY 10591 USA

Contact: Fatima Pacheco
Regulatory Clinical Affairs Specialist
Phone: (914) 524-2450
Fax: (914) 524-3579
E-mail: fatima.pacheco@siemens.com

Date Prepared: March 25, 2015

II. DEVICE

Name of Device: ADVIA Centaur® Cortisol (COR) Assay

Regulatory Information:

Product Code	Classification	Regulation	Panel
JFT	Class II	21 CFR 862.1250 Cortisol (hydrocortisone and hydroxycorticosterone) test system	Clinical Chemistry (75)

III. PREDICATE DEVICE

Name of Device: ADVIA Centaur® Cortisol (COR) Assay

510 (k): k962559

IV. DEVICE DESCRIPTION

The ADVIA Centaur Cortisol assay is a competitive immunoassay using direct chemiluminescent technology. Results are determined using a calibration curve that is generated specifically on each instrument by a 2-point calibration and a master curve with the reagent bar code. The ADVIA Centaur Cortisol Assay is intended for use on the ADVIA Centaur Family of analyzers. The ADVIA Centaur Calibrator E is a set of 2 level calibrators for the assay. Siemens recommends the use of commercially available quality control materials with at least two levels (low and high).

The ADVIA Centaur COR reagent kit contains the following:

- ADVIA Centaur ReadyPack® primary reagent pack contains Lite Reagent and Solid Phase Reagent

Materials Required but Not provided

- ADVIA Centaur Calibrator E: consists of 2 levels (low and high) of multi-analyte calibrators; lyophilized human plasma spiked with analytes (cortisol, progesterone, and testosterone), sodium azide (0.1%) and preservatives.

Optional Reagents

- ADVIA Centaur Multi-Diluent 3 is a human plasma solution with sodium azide (0.1%)
- ADVIA Centaur COR Master Curve Material is a set of 7 levels of cortisol (MCM1-7) spiked in lyophilized human plasma and sodium azide (0.1%).
- Cortisol Urine Reconstitution Buffer is a protein buffer solution with sodium azide (0.1%).

V. INDICATIONS FOR USE

The ADVIA Centaur Cortisol assay is for *in vitro* diagnostic use in the quantitative determination of cortisol in serum or urine using the ADVIA Centaur XP system. Measurements of cortisol are used in the diagnosis and treatment of disorders of the adrenal gland.

VI. INTENDED USE

Same as Indications for Use

Special Conditions for Use Statement(s): For prescription use only
Special Instrument Requirements: ADVIA Centaur® XP System

VII. COMPARISION OF TECHNOLOGICAL CHARACTERISTICS WITH THE PREDICATEDEVICE

The following table provides a comparison between the unmodified predicate ADVIA Centaur COR assay and the modified ADVIA Centaur COR assay (new antibody pool).

Table 1: *Substantial Equivalence Comparison*

Trade Name	**Candidate Device**	**Predicate Device**
	ADVIA Centaur® Cortisol (COR) Assay – Modified Device	**ADVIA Centaur® Cortisol (COR) Assay**
Intended Use	For *in vitro* diagnostic use in the quantitative determination of cortisol in serum or urine using the ADVIA Centaur XP system.	Same
Measurement	Quantitative	Same
Sample Type	Serum, Urine	Same
Assay Range	Serum: 0.50–75 µg/dL Urine: 0.50–53 µg/dL	0.20–75µg/dL
Operating Principle	Competitive immunoassay	Same
Technology	Direct chemiluminescent	Same
Sample Type	Serum, Urine	Same
Sample Volume	20 µL (serum)	Same
Standardization	Internal Standards traceable to GCMS	Same
Calibration	2-point	Same
Calibrator/Levels	Calibrator E/2 levels	Same
Controls/Levels	Commercial Controls /3 levels	Same
Master Curve Materials	Seven levels (MCM1–7)	Same
Detection Mechanism	cortisol labeled with acridinium ester	Same
Capture Antibody	polyclonal rabbit anti-cortisol antibody in the Solid Phase	Same
Reagent Storage Temperature	2–8°C	Same

VIII. Standard/Guidance Document Reference

- Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition (EP05-A2).
- Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach; Approved Guideline-First Edition (EP06-A).
- Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition (EP07-A2).

- Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline- Second Edition (EP17-A2).
- Defining, Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition (EP28-A3c).

XI. TEST PRINCIPLE

The ADVIA Centaur Cortisol assay is a competitive immunoassay using direct chemiluminescent technology. Cortisol in the patient sample competes with acridinium ester labeled cortisol in the Lite Reagent for binding to polyclonal rabbit anti-cortisol antibody in the Solid Phase. The polyclonal rabbit anti-cortisol antibody is bound to monoclonal mouse anti-rabbit antibody, which is covalently coupled to paramagnetic particles in the Solid Phase.

X. PERFORMANCE CHARATERISTICS DATA

The following data represents typical performance for the ADVIA Centaur Cortisol Assay. The data was collected on the ADVIA Centaur XP system. Substantial equivalence was demonstrated by testing several performance characteristics including imprecision, interfering and cross-reacting substances, and method comparison. All the studies evaluated produced acceptable results when compared to the Predicate and were deemed verified.

1. Precision

A 20-day precision study was performed according to CLSI EP05-A2. The samples consisted of calibrators, controls, serum, and urine pools. Each sample was tested in 2 replicates per run, 2 runs per day for 20 days for a total of 80 replicates. Results from a representative lot are presented below.

Sample	Mean (µg/dL)	Repeatability		Within Lab	
		SD	%CV	SD	%CV
Serum Control 1	2.8	0.10	3.7	0.16	6.0
Serum Control 2	22.3	0.65	2.9	1.00	4.5
Serum Control 3	34.2	1.16	3.4	1.50	4.4
Serum 1	5.7	0.19	3.3	0.30	5.3
Serum 2	50.5	2.10	4.2	2.49	4.9
Direct Urine 1	9.2	0.40	4.3	0.63	6.8
Direct Urine 2	25.6	0.91	3.5	1.73	6.8
Direct Urine 3	50.2	1.99	4.0	4.59	9.1
Extracted Urine 1	9.8	0.33	3.3	0.67	6.8
Extracted Urine 2	26.9	0.99	3.7	1.92	7.2
Extracted Urine 3	40.4	2.12	5.3	3.47	8.6
Extracted Urine 4	51.1	2.97	5.8	4.69	9.2

2. Linearity/Assay Range

A linearity study was performed across the assay measuring range 0.50–75 µg/dL. The samples were prepared using patient serum and urine samples. Linearity of the ADVIA Centaur COR assay was assessed according to EP06-A by evaluating equally spaced dilutions across the assay range. The patient serum and urine samples were assayed in triplicate and the mean of triplicate results was used for the analyses. Results of %recovery of all the serum samples are summarized below:

Serum Level	Expected (µg/dL)	Observed Mean (µg/dL)	% Recovery (Observed vs Expected)	Fitted Results		
				Linear	Fitted	% Deviation
1	0.50	0.48	96.0	0.48	0.48	1
2	10.38	10.14	97.7	10.91	10.29	-7.61
3	20.25	21.83	107.8	21.35	21.00	2.20
4	30.13	32.94	109.3	31.78	32.17	3.50
5	40.00	42.08	105.2	42.22	43.36	-0.34
6	49.88	54.14	108.5	52.66	54.11	2.75
7	59.75	64.0	107.1	63.09	64.00	1.39
8	69.63	72.81	104.6	73.53	72.58	-0.98
9	79.50	79.31	99.8	83.96	79.40	-5.87

The observed vs. expected linear regression analysis for all samples generated a weighted linear fit regression as follows:

$Y= 1.057x – 0.051$, $r^2=0.9991$

Results of % recovery of all the extracted urine samples are summarized below:

Extracted Urine Level	Expected X (µg/dL)	Observed Mean Y (µg/dL)	% Recovery (Observed vs Expected)	Fitted Result		
				Linear	Fitted	%Bias (observed v/s Linear fit)
1	0.38	0.37	97.4	0.36	0.36	0.8
2	1.50	1.24	82.7	1.39	1.39	-10.7
3	10.9	11.0	100.9	9.97	9.97	10.2
4	20.3	19.73	97.2	18.56	18.56	6.2
5	29.7	27.89	93.9	27.14	27.14	2.7
6	39.1	37.21	95.17	35.72	35.72	4.1
7	48.5	43.6	89.9	44.31	44.31	-1.7
8	57.9	52.30	90.3	52.89	52.89	-1.2
9	67.2	61.23	91.1	61.47	61.47	-0.3
10	76.6	72.92	95.2	70.06	70.06	4.1

The observed vs. expected linear regression analysis for all samples generated a weighted linear fit regression as follows:
Y= 0.914x +0.017, r^2=0.9997

Results of % recovery of all the direct urine samples are summarized below:

Direct Urine Level	Expected X (µg/dL)	Observed Mean Y (µg/dL)	% Recovery (Observed vs Expected)	Fitted Result		
				Linear	Fitted	% Deviation from fitted
1	0.46	0.55	119.6	0.55	0.54	-1.11
2	4.58	4.56	99.6	4.72	5.19	-3.60
3	10.68	11.24	105.2	10.90	11.86	3.08
4	16.79	18.49	110.1	17.07	18.24	7.69
5	22.90	24.24	105.9	23.25	24.35	4.10
6	29.01	29.88	103.0	29.42	30.18	1.53
7	35.11	35.68	101.6	35.60	35.73	0.22
8	41.22	41.71	101.2	41.77	41.01	-0.16
9	47.33	45.64	96.4	47.95	46.02	-5.05
10	53.43	50.59	94.7	54.13	50.74	-6.98

The observed vs. expected linear regression analysis for all samples generated a weighted linear fit regression as follows:
Y= 1.011x +0.090, r^2=0.9975

The linearity study supports the sponsor's claim that the measuring range of ADVIA Centaur COR assay is 0.50–75 µg/dL (serum) and 0.50–53 µg/dL (urine).

3. Analytical Detection Limits

The estimations of the Limit of Blank (LoB), Limit of Detection (LoD), and Limit of Quantitation (LoQ) were performed according to CLSI guideline EP17-A2.

Limit of Blank (LoB) was determined by calculating the 95th percentile of distribution of the test values of 6 blank samples, assayed in 5 replicates per day over 3 days (n=90).
The Limit of Detection (LoD) is the smallest amount that the assay can reliably detect to determine presence or absence of an analyte. The LoD was determined using five low cortisol serum samples tested over 3 days, 5 replicates per day (n=75).
The Limit of Quantitation (LoQ) was determined from the precision profile as the concentration of the analyte having a predicted with-in laboratory CV of 20% and not less than the LoD. Six samples with GCMS assigned doses were tested over 3 days, in 5 replicates (n=60). The LoB/LoD/LoQ estimates are summarized below:

	Serum	Direct Urine	Extracted Urine
LoB	0.06 µg/dL (1.7 nmol/L)	0.19 µg/dL (5.2 nmol/L)	0.18 µg/dL (5.0 nmol/L)
LoD	0.14 µg/dL (3.9 nmol/L)	0.45 µg/dL (12.4 nmol/L)	0.44 µg/dL (12.1 nmol/L)
LoQ	0.31 µg/dL (8.6 nmol/L)	0.48 µg/dL (13.2 nmol/L)	0.44 µg/dL (12.1 nmol/L)

The measuring range of the ADVIA Centaur COR assay is 0.50–75 µg/dL (serum) and 0.50–53 µg/dL (urine).

4. Analytical Specificity

Endogenous Interference: The effect on quantitation of analyte in the presence of endogenous substances using the ADVIA Centaur COR assay was determined. Potential interfering substances in serum and urine (24-hr direct urine) were evaluated with an acceptable % Interference ≤ 10%. Each potential interfering substances was spiked with into 2 sample pools at different concentration of the analyte targeted approximately at 5µg/dL and 30 µg/dL. The same sample pools were used as controls for each interferent by adding equivalent volumes of the appropriate solvent or diluent originally used to dissolve individual interferents. All samples were run in triplicate with one reagent lot. The results of testing at the highest dose of the endogenous substance without interference effects on analyte quantitation are summarized below:

Endogenous Substance	Low Cortisol			High Cortisol		
	Dose Without Endogenous Substance (µg/dL)	Dose With Endogenous Substance (µg/dL)	% Interference	Dose Without Endogenous Substance (µg/dL)	Dose With Endogenous Substance (µg/dL)	% Interference
Serum Cortisol Measurement						
Hemoglobin (500 mg/dL)	4.96	4.83	-3%	23.38	23.64	1%
Triglycerides (1500 mg/dL)	4.78	4.89	2%	22.82	23.08	1%
Conjugated Bilirubin (20 mg/dL)	5.82	5.69	-2%	28.56	27.30	-4%
Unconjugated Bilirubin (20 mg/dL)	4.81	5.07	5%	20.67	21.19	3%
Urine Cortisol Measurement						
Protein (60 mg/dL)	6.27	6.49	3%	21.29	21.68	2%
Sodium Chloride 1 M (5844 mg/dL)	6.57	6.22	-5%	21.35	20.26	-5%
Urea 350 mM	6.60	6.40	-3%	21.25	21.42	1%

Endogenous Substance	Low Cortisol			High Cortisol		
	Dose Without Endogenous Substance (µg/dL)	Dose With Endogenous Substance (µg/dL)	% Interference	Dose Without Endogenous Substance (µg/dL)	Dose With Endogenous Substance (µg/dL)	% Interference
(2102 mg/dL)						
Creatinine 5 mM (56.6 mg/dL)	6.27	6.28	0%	21.28	21.87	3%
Glucose 2 mM (36 mg/dL)	6.41	6.43	0%	21.36	21.74	2%
Boric Acid 10g/dL	6.48	6.53	1%	21.51	21.67	1%

Cross-reactivity: The specificity of the modified ADVIA Centaur COR assay was determined using two human serum sample pools spiked with potential cross-reactant compounds. The sample analyte concentrations were approximately 0 and ~5 µg/dL cortisol. Potential cross reactants were spiked into each sample at concentrations 50–1000 µg/dL for cross-reactivity evaluation. The spiked and unspiked samples were tested in triplicate. The cross-reactivity results are summarized in the table below:

Cross reactant Tested	Concentration Tested	% Cross-reactivity
Aldosterone	1,000 µg/dL	0.4
Allotetrahydrocortisol	100 µg/dL	11.9
Androstenedione	1,000 µg/dL	0.2
Corticosterone	1,000 µg/dL	2.6
Cortisone	100 µg/dL	11.5
α-Cortol	1,000 µg/dL	0.6
α-Cortolone	1,000 µg/dL	0.1
β-Cortol	1,000 µg/dL	0.1
β-Cortolone	1,000 µg/dL	0.0
Dehydrocorticosterone	1,000 µg/dL	2.7
11-deoxycorticosterone	1,000 µg/dL	0.9
11-deoxycortisol	100 µg/dL	18.3
21-deoxycortisol	100 µg/dL	10.3
20 α-dihydrocortisol	1,000 µg/dL	2.5
20 β-dihydrocortisol	1,000 µg/dL	2.5
20 α-dihydrocortisone	1,000 µg/dL	0.5

Cross reactant Tested	Concentration Tested	% Cross-reactivity
20 β-dihydrocortisone	1,000 µg/dL	0.3
11 β-hydroxyandrosterone	1,000 µg/dL	0.0
6-β hydroxycortisol	1,000 µg/dL	2.3
11 β-hydroxyetiocholanone	1,000 µg/dL	0.0
11 β-hydroxyprogesterone	1,000 µg/dL	1.0
17α-hydroxyprogesterone	1,000 µg/dL	1.4
17α-hydroxypregnenolone	1,000 µg/dL	0.1
11-keto-androsterone	1,000 µg/dL	0.0
11-keto-etiochalanonlone	1,000 µg/dL	0.0
Pregnanetriol	1,000 µg/dL	0.0
Pregnenolone	1,000 µg/dL	0.1
Progesterone	1,000 µg/dL	0.5
Spironolactone	1,000 µg/dL	0.1
Testosterone	1,000 µg/dL	0.3
Tetrahydrocortisol	1,000 µg/dL	1.1
Tetrahydrocortisone	1,000 µg/dL	0.5
Tetrahydro-11-deoxycortisol	1,000 µg/dL	0.7
Prednisolone	50 µg/dL	92
6-methyl-prednisolone	100 µg/dL	23.1
Dexamethasone	1,000 µg/dL	0.5
Prednisone	100 µg/dL	10.7
Canrenone	1,000 µg/dL	0.2

5. Expected Values (Reference Intervals)

A reference interval study was performed according to CLSI EP28-A3c using the ADVIA Centaur COR assay on 252 serum samples from apparently healthy male and female individuals. Based on a central 95% interval, the following reference intervals were established:

Sample Category	N	Reference Intervals	
		(µg/dL)	(nmol/L)
AM Serum (7–9 AM)	127	5.27–22.45	145.4–619.4
PM Serum (3–5 PM)	125	3.44–16.76	94.9–462.4

Reference intervals for 24 hour direct urine and extracted urine, previously established with the unmodified predicate ADVIA Centaur COR assay, were verified for the modified ADVIA Centaur COR assay following the protocol established by CLSI EP28-A3c. For the verification study24-hour direct urine specimens (n=20) and 24-hour extracted urine. Since ≤10% of specimens fell outside of the previously-established reference intervals, the existing claim continues to be valid.

Sample Category	N	Reference Intervals	
		(µg/24-hr)	(nmol/24-hr)
Direct Urine	105	20.9–292.3	57.7–806.8
Extracted Urine	105	9.5–136.2	26.2–375.9

Siemens provides this information for reference. As with all *in vitro* diagnostic assays, each laboratory should determine its own reference ranges for the diagnostic evaluation of patient results.

6. Method Comparison with predicate device

Method comparison studies were performed by comparing the modified device to the currently-marketed predicate device (unmodified ADVIA Centaur COR assay) with two-hundred and forty-three (243) serum samples, ninety-eight (98) 24-hour direct urine, and one-hundred and eleven (111) distributed over the assay range. The analysis was performed using Weighted Deming regression. The regression equations and sample ranges from the analyses are presented below.

Sample Category	N	Range	Regression Equation
Serum	243	0.53–67.42 µg/dL	Modified Device= 1.00(Unmodified Device) + 0.07 µg/dL (r = 0.996)
Direct Urine	98	2.64–47.00 µg/dL	Modified Device = 1.11(Unmodified Device) + 0.68 µg/dL (r = 0.969)
Extracted Urine	111	1.13–50.69 µg/dL	Modified Device = 0.86(Unmodified Device) + 0.38 µg/dL (r = 0.991)

Based on this study data the sponsor claims sample type's serum and urine (direct and extracted) are acceptable for ADVIA Centaur COR assay.

7. Dilution Recovery

Dilution studies were performed to demonstrate that the high cortisol samples with concentrations greater the 75 µg/dL can be auto-diluted using a ratio 1:2 dilution with Multi-Diluent 3 and assayed for recovery versus a 1:2 manual dilution can be accurately measured by the ADVIA Centaur Cortisol assay. Five human serum samples in the range of 63.3–76.5 µg/dL were used and the % Recovery was determined by dividing the dose (Auto dilution) by the dose (Manual dilution). The recoveries ranged from 106–111% with a mean of 109%. Results are summarized below:

Sample ID	Auto Dilution (µg/dL)	Manual Dilution (µg/dL)	% Recovery
1	74.4	67.0	111
2	76.5	69.1	111
3	63.3	59.7	106
4	72.9	66.5	110
5	70.3	66.1	106
			Mean: 109

8. Reagent Stability

The shelf-life of the ADVIA Centaur Cortisol assay is 15 months when properly stored unopened at 2–8°C. The expiration date is printed on the carton. On-system (open packs in use) are stable for up to 10 days.

The shelf-life of the ADVIA Centaur Calibrator E is 16 months when properly stored unopened at 2–8°C; reconstituted open vial stable for 14 days; on-system stable for 4 hours. The expiration date is printed on the carton.

The shelf-life of the ADVIA Centaur Cortisol Master Curve Material is 22 months when properly stored unopened at 2–8°C; reconstituted open vial stable for 14 days; on-system stable for 4 hours. The expiration date is printed on the bag label.

9. Traceability

The ADVIA Centaur Cortisol assay is standardized using internal standards manufactured analytically which are traceable to the gas chromatography-mas spectroscopy (GC-MS). Assigned values for Calibrator E and MCMs are traceable to this standardization.

Production lots of Calibrator E are value assigned using 2 reagent lots, 6 replicates, 2 runs on 3 different ADVIA Centaur systems for a total of 72 replicates. The average dose obtained at value assignment for a new calibrator lot are the assigned values.

Production lots of ADVIA Centaur Cortisol MCMs are value assigned using assigned reference calibrators and MCMs. A nested testing protocol consisting of 20 replicates per

level using one reagent lot and one ADVIA Centaur system. The new MCM doses must fall within the final value assignment specification for COR MCMs. The MCMs dose values are generated using the two-point calibration. The new MCM dose is calculated based on the relationship between the observed reference MCM dose and its assigned value.

XI. CLINICAL STUDIES

Not applicable.

XII. CLINICAL CUT-OFF

Not applicable.

XIII. PROPOSED LABELING

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

XIV. CONCLUSION

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.